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NEWS 20 Jun 10 MEDLINE Reload  
NEWS 21 Jun 10 PCTFULL has been reloaded  
NEWS 22 Jul 02 FOREGE no longer contains STANDARDS file segment  
NEWS 23 Jul 19 NTIS to be reloaded July 28, 2002  
  
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FILE COVERS 1907 - 21 Jul 2002 VOL 137 ISS 4

FILE LAST UPDATED: 19 Jul 2002 (20020719/ED)

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=> HCV and envelope

5531 HCV

14 HCVS

5534 HCV

(HCV OR HCVS)

41663 ENVELOPE

7861 ENVELOPES

46283 ENVELOPE

(ENVELOPE OR ENVELOPES)

L1 456 HCV AND ENVELOPE

=> E1 or E2 and L1

'E1' NOT FOUND

The E# entered is not currently defined.

=> E1 and L1

'E1' NOT FOUND

The E# entered is not currently defined.

=> envelope 1 and L1

41663 ENVELOPE

7861 ENVELOPES

46283 ENVELOPE  
 (ENVELOPE OR ENVELOPES)  
 7186860 1  
 60 ENVELOPE 1  
 (ENVELOPE(W) 1)  
 L2 21 ENVELOPE 1 AND L1

=> D L2 IBIB TI SO AU ABS 1-21

L2 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:224906 CAPLUS  
 DOCUMENT NUMBER: 136:339231  
 TITLE: Early changes in hepatitis C viral quasispecies  
 during  
 interferon therapy predict the therapeutic outcome  
 AUTHOR(S): Farci, Patrizia; Strazzera, Rita; Alter, Harvey J.;  
 Farci, Stefania; Degioannis, Daniela; Coiana,  
 Alessandra; Peddis, Giovanna; Usai, Francesco; Serra,  
 Giancarlo; Chessa, Luchino; Diaz, Giacomo;  
 Balestrieri, Angelo; Purcell, Robert H.  
 CORPORATE SOURCE: Department of Medical Sciences, University of  
 Cagliari, Cagliari, 09124, Italy  
 SOURCE: Proceedings of the National Academy of Sciences of  
 the  
 United States of America (2002), 99(5), 3081-3086  
 CODEN: PNASA6; ISSN: 0027-8424  
 PUBLISHER: National Academy of Sciences  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

TI Early changes in hepatitis C viral quasispecies during interferon therapy  
 predict the therapeutic outcome  
 SO Proceedings of the National Academy of Sciences of the United States of  
 America (2002), 99(5), 3081-3086  
 CODEN: PNASA6; ISSN: 0027-8424  
 AU Farci, Patrizia; Strazzera, Rita; Alter, Harvey J.; Farci, Stefania;  
 Degioannis, Daniela; Coiana, Alessandra; Peddis, Giovanna; Usai,  
 Francesco; Serra, Giancarlo; Chessa, Luchino; Diaz, Giacomo; Balestrieri,  
 Angelo; Purcell, Robert H.  
 AB Despite recent treatment advances, the majority of patients with chronic  
 hepatitis C fail to respond to antiviral therapy. Although the genetic  
 basis for this resistance is unknown, accumulated evidence suggests that  
 changes in the heterogeneous viral population (quasispecies) may be an  
 important determinant of viral persistence and response to therapy.  
 Sequences within hepatitis C virus (HCV) **envelope**  
**1** and **envelope 2** genes, inclusive of the hypervariable  
 region 1, were analyzed in parallel with the level of viral replication  
 in  
 serial serum samples obtained from 23 patients who exhibited different  
 patterns of response to therapy and from untreated controls. Our study  
 provides evidence that although the viral diversity before treatment does  
 not predict the response to treatment, the early emergence and dominance  
 of a single viral variant distinguishes patients who will have a  
 sustained  
 therapeutic response from those who subsequently will experience a  
 breakthrough or relapse. A dramatic redn. in genetic diversity leading  
 to  
 an increasingly homogeneous viral population was a consistent feature  
 assocd. with viral clearance in sustained responders and was independent  
 of HCV genotype. The persistence of variants present before  
 treatment in patients who fail to respond or who experience a  
 breakthrough

during therapy strongly suggests the preexistence of viral strains with inherent resistance to IFN. Thus, the study of the evolution of the **HCV** quasispecies provides prognostic information as early as the first 2 wk after starting therapy and opens perspectives for elucidating the mechanisms of treatment failure in chronic hepatitis C.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L2 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:912910 CAPLUS

TITLE: Secretory expression of different C-terminal truncated

AUTHOR(S): **HCV** E1 proteins in mammalian cells and characterization of the expressed products  
Zhu, Jun; Kong, Yuying; Liu, Jing; Zhang, Zuchuan; Wang, Yuan; Li, Guangdi

CORPORATE SOURCE: Institute of Biochemistry and Cell Biology, Shanghai Institute for Biological Sciences, Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China

SOURCE: Shengwu Huaxue Yu Shengwu Wuli Xuebao (2001), 33(6), 634-640

CODEN: SHWPAU; ISSN: 0582-9879

PUBLISHER: Shanghai Kexue Jishu Chubanshe

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

TI Secretory expression of different C-terminal truncated **HCV** E1 proteins in mammalian cells and characterization of the expressed products

SO Shengwu Huaxue Yu Shengwu Wuli Xuebao (2001), 33(6), 634-640

CODEN: SHWPAU; ISSN: 0582-9879

AU Zhu, Jun; Kong, Yuying; Liu, Jing; Zhang, Zuchuan; Wang, Yuan; Li, Guangdi

AB Three fragments of **HCV** envelope 1 (E1) with different C- terminal truncation at aa310, aa325, aa340 were cloned into the mammalian expression vector pSecTagB. An epitope in the hepatitis B surface antigen, preS1(21-47), were genetically engineered onto the N-terminus of the recombinant protein and used as an affinity tag for detection and purifn. The resulting pSec-preS1-E1t310, pSec-preS1-E1t325, and pSec- preS1-E1t340 were transiently expressed in the HeLa cells and antigenicity, secretory efficiency, and glycosylation type of the recombinant E1 proteins were compared. All of the three recombinant proteins could be detected by both preS1 monoclonal antibody and E1 polyclonal antiserum. The expression products were secreted and highly mannose-type glycosylated, with S1E1t325 being secreted, indicating the influence of the hydrophobic regions on the secretion of the E1 protein. Three CHO cell lines expressing the proteins, S1E1t310, S1E1t325, and S1E1t340, were established and CHO/pSecS1E1t325 was chosen for further study. The secreted S1E1t325 could be enriched from cell culture medium by the preS1 antibody-coupled Sepharose. The glycosylation anal. indicated the lack of complex glycogen even after the E1 was secreted via Golgi complexes. The established stable cell lines and anti-preS1 affinity method could be utilized to enrich and purify the **HCV** E1 expressed in mammalian cells, and may be used for further characterization of this protein.

L2 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:888331 CAPLUS

DOCUMENT NUMBER: 136:133500  
TITLE: Hepatitis C virus core and **envelope** proteins do not suppress the host's ability to clear a hepatic viral infection  
AUTHOR(S): Sun, Jiaren; Bodola, Francis; Fan, Xuegong; Irshad, Habib; Soong, Lynn; Lemon, Stanley M.; Chan, Teh-Sheng  
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Texas Medical Branch at Galveston, Galveston, TX, 77555-1070, USA  
SOURCE: Journal of Virology (2001), 75(24), 11992-11998  
CODEN: JOVIAM; ISSN: 0022-538X  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

TI Hepatitis C virus core and **envelope** proteins do not suppress the host's ability to clear a hepatic viral infection  
SO Journal of Virology (2001), 75(24), 11992-11998  
CODEN: JOVIAM; ISSN: 0022-538X  
AU Sun, Jiaren; Bodola, Francis; Fan, Xuegong; Irshad, Habib; Soong, Lynn; Lemon, Stanley M.; Chan, Teh-Sheng  
AB Several hepatitis C virus (HCV) proteins have been shown in vitro to interact with host cellular components that are involved in immune regulation. However, there is a paucity of data supporting the relevance of these observations to the in vivo situation. To test the hypothesis that such an interaction suppresses immune responses, the authors studied a line of transgenic C57BL/6 mice that express the **HCV** core and **envelope** proteins in the liver. The potential effects of these proteins on the hepatic immune response were evaluated by challenging these mice with a hepatotropic adenovirus. Both transgenic and nontransgenic mice developed similar courses of infection and cleared the virus from the liver by 28 days post-infection. Both groups of mice mounted similar IgG, IgG2a, interleukin-2, and tumor necrosis factor alpha responses against the virus. Addnl., BALB/c mice does not express the **HCV** core and **envelope** 1 proteins in the same manner. These data suggest that **HCV** core and **envelope** proteins do not inhibit the hepatic antiviral mechanisms in these murine exptl. systems and thus favor a model in which **HCV** circumvents host responses through a mechanism that does not involve general suppression of intrahepatic immune responses.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L2 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:445658 CAPLUS  
DOCUMENT NUMBER: 136:178463  
TITLE: Investigating hepatitis C virus heterogeneity in a high prevalence setting using heteroduplex tracking analysis  
AUTHOR(S): Sullivan, D. G.; Kim, S. S.; Wilson, J. J.; Stehman-Breen, C.; Gretch, D. R.  
CORPORATE SOURCE: Department of Laboratory Medicine, University of Washington Medical Center, Seattle, WA, 98104-2499, USA  
SOURCE: Journal of Virological Methods (2001), 96(1), 5-16  
CODEN: JVMEDH; ISSN: 0166-0934

PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
TI Investigating hepatitis C virus heterogeneity in a high prevalence setting  
using heteroduplex tracking analysis  
SO Journal of Virological Methods (2001), 96(1), 5-16  
CODEN: JMVMDH; ISSN: 0166-0934  
AU Sullivan, D. G.; Kim, S. S.; Wilson, J. J.; Stehman-Breen, C.; Gretch, D. R.  
AB Hepatitis C virus (HCV) infection is very common among chronic hemodialysis patients. In the past, blood transfusion appeared to be the primary risk factor; however evidence of nosocomial HCV transmission in the hemodialysis setting has recently been reported.

This report describes a mol. investigation of HCV isolates obtained from a population of 670 patients attending six different Seattle-King County based hemodialysis centers in order to identify potential common source infections. Seven hundred thirty-three serum specimens were collected from hemodialysis patients in 1992 and 1996, and were tested for HCV antibodies and RNA. Overall, 115 of 670 (17%) patients were pos. for HCV RNA, and thus were considered actively infected by HCV. HCV genotype was detd. in all cases by restriction fragment length polymorphism, and 93 patients were found to be infected by HCV genotype 1. HCV envelope genes were amplified from the 93 patients with genotype 1 infection, and were studied in further detail by heteroduplex tracking anal. (HTA) using genotype 1a and 1b specific probes derived from the envelope 1 (E1) and envelope 2 (E2) genes. Genetic relatedness between pairs of HCV envelope genes was estd. by calcg. the degree of gel shift relative to homoduplex controls. Nucleotide sequencing and phylogenetic anal. was used to confirm genetic relatedness detected by HTA. When HTA was performed using the E1 gene probe, 12 apparently related infections were detected; 10 of 12 (83%) of these infections were confirmed as truly related using the gold std. method of nucleotide sequencing plus phylogenetic anal. Using an E2 gene probe, 24 infections were apparently related, but only six (25%) were confirmed by sequencing. As a control, 41 envelope genes, which were unrelated by HTA, were sequenced; 0 of 41 (0%) were truly related. In summary, HTA provides a rapid and effective mol. technique for screening HCV genetic relatedness in population-based studies, and should prove valuable in future studies of HCV mol. epidemiol.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L2 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:328609 CAPLUS  
DOCUMENT NUMBER: 135:353459  
TITLE: Prokaryotic expression of hepatitis C virus envelope 1 gene and application of expressed product  
AUTHOR(S): Gao, Jian'en; Tao, Qimin; Ma, Dalong; Feng, Baifang; Ji, Heping; Ji, Ying  
CORPORATE SOURCE: Hepatology Institute of Beijing Medical University, People's Hospital, Beijing, 100044, Peop. Rep. China

SOURCE: Zhonghua Shiyan He Linchuang Bingduxue Zazhi (2001),  
15(1), 20-23  
CODEN: ZSLZFS; ISSN: 1003-9279  
PUBLISHER: Zhonghua Shiyan He Linchuang Bingduxue Zazhi Bianjibu  
DOCUMENT TYPE: Journal  
LANGUAGE: Chinese

TI Prokaryotic expression of hepatitis C virus **envelope 1**  
gene and application of expressed product  
SO Zhonghua Shiyan He Linchuang Bingduxue Zazhi (2001), 15(1), 20-23  
CODEN: ZSLZFS; ISSN: 1003-9279  
AU Gao, Jian'en; Tao, Qimin; Ma, Dalong; Feng, Baifang; Ji, Heping; Ji, Ying  
AB The **HCV** E1 gene was expressed in *E. coli*. The expression vector  
was constructed by ligation of **HCV** E1 sequence, which was  
amplified by RT-PCR methods from 50 .mu.l of **HCV** RNA pos. serum  
using primers specific to the **HCV** E1 sequence, to the  
prokaryotic expression vector PMS-31b transfected POP2136 at 16.degree.  
for 16 h. The recombinant plasmid was screened out and characterized by  
restriction enzyme anal. The bacteria contg. the recombinant plasmid was  
induced at 42.degree. for 4 h, and the recombinant protein was visualized  
by SDS-PAGE. The specificity of the recombinant protein was detd. by  
Western blot assay. After purifn. of the expressed protein, this protein  
was coated on the plate with the concn. of 2 .mu.g/mL in pH 9.6 buffer at  
4.degree. for overnight, and the serum specimen was tested at the diln.

of 1:20 by ELISA. Two fragments could be seen on the SDS-PAGE after  
digestion of the RT-PCR product with SmaI. And there emerged one  
fragment of 356 bp after digesting the recombinant plasmid with SmaI and XbaI. A  
band of 30,000 could be seen on the SDS-PAGE after the induction of  
bacteria contg. the recombinant plasmid pMS-E1 at 42.degree. for 4 h.

The ELISA result indicated that 28.9% (26/90) anti-**HCV** pos. serum  
were anti-**HCV** E1 pos., but 3.9% (3/76) were pos. in the anti-  
**HCV** neg. serum. The **HCV** E1 sequence from **HCV**  
RNA pos. serum has been expressed in *E. coli*. The expression rate is  
about 17% of the total protein of the bacteria. This protein possessed  
good specificity and may be used in the diagnosis of **HCV**  
infection.

L2 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:212987 CAPLUS  
DOCUMENT NUMBER: 136:1134  
TITLE: Genome of human hepatitis C virus (**HCV**):  
Gene organization, sequence diversity, and variation  
AUTHOR(S): Kato, Nobuyuki  
CORPORATE SOURCE: Department of Molecular Biology, Institute of  
Cellular

and Molecular Biology, Okayama University Medical  
School, Okayama, 700-8558, Japan  
SOURCE: Microbial & Comparative Genomics (2000), 5(3),  
129-151

CODEN: MCGEFP; ISSN: 1090-6592  
PUBLISHER: Mary Ann Liebert, Inc.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

TI Genome of human hepatitis C virus (**HCV**): Gene organization,  
sequence diversity, and variation  
SO Microbial & Comparative Genomics (2000), 5(3), 129-151  
CODEN: MCGEFP; ISSN: 1090-6592  
AU Kato, Nobuyuki

AB A review with refs. Hepatitis C virus (HCV) is the major etiol. agent of non-A, non-B hepatitis. HCV infection frequently causes chronic hepatitis, which progresses to liver cirrhosis and hepatocellular carcinoma. Since the discovery of HCV in 1989, a large no. of genetic analyses of HCV have been reported, and the viral genome structure has been elucidated. An enveloped virus, HCV belongs to the family Flaviviridae, whose genome consists of a pos.-stranded RNA mol. of about 9.6 kilobases and encodes a large polyprotein precursor (about 3000 amino acids). This precursor protein is

cleaved by the host and viral proteinase to generate at least 10 proteins:

the core, **envelope 1** (E1), E2, p7, nonstructural (NS) 2, NS3, NS4A, NS4B, NS5A, and NS5B. These HCV proteins not only function in viral replication but also affect a variety of cellular functions. HCV has been found to have remarkable genetic heterogeneity. To date, more than 30 HCV genotypes have been identified worldwide. Furthermore, HCV may show quasispecies distribution in an infected individual. These findings may have important implications in diagnosis, pathogenesis, treatment, and vaccine development. The hypervariable region 1 found within the **envelope** E2 protein was shown to be a major site for the genetic evolution of HCV after the onset of hepatitis, and might be involved in escape from the host immunosurveillance system.

REFERENCE COUNT: 241 THERE ARE 241 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L2 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:892533 CAPLUS

DOCUMENT NUMBER: 135:57401

TITLE: Expression and membrane association of hepatitis C virus **envelope 1** protein

AUTHOR(S): Ciccaglione, Anna Rita; Marcantonio, Cinzia; Costantino, Angela; Equestre, Michele; Geraci, Andrea;

Rapicetta, Maria

CORPORATE SOURCE: Laboratory of Virology, Istituto Superiore di Sanita, Rome, 00161, Italy

SOURCE: Virus Genes (2000), 21(3), 223-226

CODEN: VIGEET; ISSN: 0920-8569

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

TI Expression and membrane association of hepatitis C virus **envelope 1** protein

SO Virus Genes (2000), 21(3), 223-226

CODEN: VIGEET; ISSN: 0920-8569

AU Ciccaglione, Anna Rita; Marcantonio, Cinzia; Costantino, Angela; Equestre,

Michele; Geraci, Andrea; Rapicetta, Maria

AB The expression of hepatitis C virus (HCV) E1 protein is toxic for Escherichia coli cells. For this reason, we have cloned the E1 gene in the pET3a vector and analyzed the inducible expression of the protein in two strains of E. coli characterized by a different level of redn. of basal synthesis. The results indicated that synthesis of E1 was supported

only by the BL21(DE3)pLysS strain which provides a tightest control of protein expression before the induction. The BL21(DE3)pLysS cells were



then used for the expression of E1 gene, varying at its carboxy terminus in order to retain (E1, aa 192-383) or delete (E1t, aa 192-340) a C-terminal hydrophobic region that may be involved in membrane assocn. Following cell fractionation, E1 protein was found assocd. with the membrane fraction. By contrast, the truncated mutant E1t, was identified in the sol. phase suggesting a direct role for the C-terminal domain in

E1

membrane assocn.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L2 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:419879 CAPLUS

DOCUMENT NUMBER: 133:307447

TITLE: A novel hepatitis C virus (HCV) subtype from Somalia and its classification into HCV clade 3

AUTHOR(S): Abid, Karim; Quadri, Rafael; Veuthey, Anne-Lise; Hadengue, Antoine; Negro, Francesco

CORPORATE SOURCE: Division of Gastroenterology and Hepatology, University Hospital, Geneva, 1211, Switz.

SOURCE: Journal of General Virology (2000), 81(6), 1485-1493

CODEN: JGVIAY; ISSN: 0022-1317

PUBLISHER: Society for General Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

TI A novel hepatitis C virus (HCV) subtype from Somalia and its classification into HCV clade 3

SO Journal of General Virology (2000), 81(6), 1485-1493

CODEN: JGVIAY; ISSN: 0022-1317

AU Abid, Karim; Quadri, Rafael; Veuthey, Anne-Lise; Hadengue, Antoine; Negro, Francesco

AB Hepatitis C virus (HCV) sequences from throughout the world have been grouped into six clades, based on recently proposed criteria. Here, the partial sequences and clade assignment are reported for three HCV isolates from chronic hepatitis C patients from Somalia, for whom conventional assays failed to identify the genotype. Phylogenetic anal. of the sequences of the core, envelope 1 and part of the non-structural 5b regions suggests that all three isolates belong to a distinct HCV genetic group, tentatively classified as subtype 3h. This novel HCV subtype shows the highest sequence similarity with HCV isolates from Indonesia. Despite the fact that these patients were infected with HCV clade 3, none of them responded to std. interferon treatment.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE  
FORMAT

L2 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:413510 CAPLUS

DOCUMENT NUMBER: 131:209940

TITLE: Why is the interferon sensitivity-determining region (ISDR) system useful in Japan?

AUTHOR(S): Nakano, Isao; Fukuda, Yoshihide; Katano, Yoshiaki;

CORPORATE SOURCE: Nakano, Satoshi; Kumada, Takashi; Hayakawa, Tetsuo  
Second Department of Internal Medicine, Nagoya

Japan  
 SOURCE: University School of Medicine, Nagoya, 466-8550,  
 Journal of Hepatology (1999), 30(6), 1014-1022  
 CODEN: JOHEEC; ISSN: 0168-8278  
 PUBLISHER: Munksgaard International Publishers Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

TI Why is the interferon sensitivity-determining region (ISDR) system useful  
 in Japan?  
 SO Journal of Hepatology (1999), 30(6), 1014-1022  
 CODEN: JOHEEC; ISSN: 0168-8278  
 AU Nakano, Isao; Fukuda, Yoshihide; Katano, Yoshiaki; Nakano, Satoshi;  
 Kumada, Takashi; Hayakawa, Tetsuo  
 AB The amino acid sequence of NS5A2209-2248, named the "interferon  
 sensitivity-detg. region" (ISDR), has been reported to correlate with  
 responsiveness of interferon (IFN) therapy to patients with the hepatitis  
 C virus (HCV) genotype-1b, by several Japanese authors.  
 However, European authors have failed to find this phenomenon, suggesting  
 a difference in HCV-1b isolates between Japan and Europe. We  
 compared the HCV-1b nucleotide sequences of our Japanese  
 patients and those of other countries quoted from GenBank, using the  
**envelope 1** sequence. A phylogenetic tree anal. revealed  
 two characteristic groups from a geog. viewpoint: one group (NJ group)  
 consists of almost entirely non-Japanese isolates, and the other (J  
 group)  
 of almost entirely Japanese isolates. The isolates other than the NJ and  
 J groups are characterized by their specific nucleotide residue,  
 constructing an individual group (W group). Japanese HCV-1b  
 isolates consist of the J group and W group (approx. 40% and 60%, resp.).  
 Comparative study between the two groups in Japanese patients treated  
 with  
 IFN revealed a strong correlation between ISDR type and IFN  
 responsiveness  
 only in the J group, but not in the W group. These observations  
 convinced  
 us that the existence of the Japan-specific J group is one reason why the  
 ISDR system is useful only in Japan.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR  
 THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE  
 FORMAT

L2 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1997:67576 CAPLUS  
 DOCUMENT NUMBER: 126:129053  
 TITLE: Classification of hepatitis C virus variants in six  
 major types based on analysis of the **envelope**  
**1** and nonstructural 5B genome regions and  
 complete polyprotein sequences  
 AUTHOR(S): de Lamballerie Xavier; Charrel, Remi N.; Attoui,  
 Houssam; De Micco, Philippe  
 CORPORATE SOURCE: Faculte Medecine, Hopital Timone, Marseille, 13385,  
 Fr.  
 SOURCE: Journal of General Virology (1997), 78(1), 45-51  
 CODEN: JGVIAV; ISSN: 0022-1317  
 PUBLISHER: Society for General Microbiology  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

TI Classification of hepatitis C virus variants in six major types based on  
 analysis of the **envelope 1** and nonstructural 5B genome

regions and complete polyprotein sequences

SO Journal of General Virology (1997), 78(1), 45-51  
CODEN: JGVIAY; ISSN: 0022-1317

AU de Lamballerie Xavier; Charrel, Remi N.; Attoui, Houssam; De Micco, Philippe

AB The phylogenetic status of recently described isolates of hepatitis C virus (HCV) from Vietnam, Thailand and Indonesia (previously classified as types 7, 8, 9, 10 and 11) was re-analyzed by the neighbor-joining method instead of the unweighted pair-group method with arithmetic mean (UPGMA) that was first used by the discoverers of these strains. The anal. of complete amino acid sequences and of nucleotide sequences of the **envelope 1** (672 nt) and nonstructural 5B (1092 nt) genomic regions permitted the re-assignment of the type 7, 8, 9 and 11 isolates to type 6, and that of type 10 strains to type 3. Finally, this study made possible the classification of the previously described HCV strains (including these South-East Asian isolates) in six major types and at least 30 subtypes. It confirms that anal. of the E1 and NS5B genomic regions using the neighbor-joining method is a reliable tool for the assignment of most new isolates.

L2 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:637827 CAPLUS

DOCUMENT NUMBER: 125:325919

TITLE: Treatment with recombinant interferon-.alpha.2a for patients with chronic hepatitis C: predictive factors for biochemical and virologic response

AUTHOR(S): Hagiware, H.; Hayashi, N.; Kasahara, A.; Oshita, M.; Katayama, K.; Kato, M.; Masuzawa, M.; Fusamoto, H.; Sakurai, M.; et al.

CORPORATE SOURCE: First Dept. Med., Osaka Univ. School of Medicine, Osaka, Japan

SOURCE: Scand. J. Gastroenterol. (1996), 31(10), 1021-1026  
CODEN: SJGRA4; ISSN: 0036-5521

DOCUMENT TYPE: Journal

LANGUAGE: English

TI Treatment with recombinant interferon-.alpha.2a for patients with chronic hepatitis C: predictive factors for biochemical and virologic response

SO Scand. J. Gastroenterol. (1996), 31(10), 1021-1026  
CODEN: SJGRA4; ISSN: 0036-5521

AU Hagiware, H.; Hayashi, N.; Kasahara, A.; Oshita, M.; Katayama, K.; Kato, M.; Masuzawa, M.; Fusamoto, H.; Sakurai, M.; et al.

AB The heterogeneity of the hepatitis C virus (HCV) genome has been reported to be assocd. with the effectiveness of interferon therapy. We investigated the correlation of the viral and host factors, including the degree of sequence complexity of the HCV genome for responses to interferon-.alpha. in patients with chronic hepatitis C. Ninety-seven patients received a 26-wk course of recombinant interferon-.alpha.2a therapy. The sequence complexity of the **envelope 1-2** region was evaluated by polymerase chain reaction-mediated single-strand conformation polymorphism (PCR-SSCP) anal. Of the 85 patients who completed the treatment, 31 (36%) achieved a sustained response, and 28 (33%) showed a sustained loss of HCV RNA. A low HCV RNA level, detd. by the branched DNA probe assay, and serotype group 2 HCV correlated with a sustained response. In patients with serotype group 1 HCV of more than the threshold of the branched DNA probe assay, a band no. on PCR-SSCP anal. of more than 2 could be assocd. with inefficacy of interferon therapy. Multivariate anal. in the 50 patients whose sera were available for all the virol. tests showed that

only the **HCV** RNA level is independently predictive of a sustained response. Detn. of the **HCV** RNA level is most important for predicting the response before interferon therapy.

PCR-SSCP

anal. may be useful as an addnl. test for patients with a high **HCV** RNA level of serotype group 1 **HCV**.

L2 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:336531 CAPLUS

DOCUMENT NUMBER: 125:5386

TITLE: Nucleotide and amino acid sequences of the **envelope 1** and core genes of hepatitis C virus isolates

INVENTOR(S): Bukh, Jens; Miller, Roger H.; Purcell, Robert H.

PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA

SOURCE: PCT Int. Appl., 338 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9605315	A2	19960222	WO 1995-US10398	19950815
WO 9605315	A3	19960404		
W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT			
RW:	KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
US 5882852	A	19990316	US 1994-290665	19940815
AU 9534065	A1	19960307	AU 1995-34065	19950815
AU 712385	B2	19991104		
EP 779924	A2	19970625	EP 1995-930831	19950815
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE			

SE

PRIORITY APPLN. INFO.:

US 1994-290665	A	19940815
US 1993-86428	A2	19930629
WO 1995-US10398	W	19950815

TI Nucleotide and amino acid sequences of the **envelope 1** and core genes of hepatitis C virus isolates

SO PCT Int. Appl., 338 pp.

CODEN: PIXXD2

IN Bukh, Jens; Miller, Roger H.; Purcell, Robert H.

AB The nucleotide and deduced amino acid sequences of cDNAs encoding the **envelope (1)** genes and core genes of isolates of hepatitis C virus (**HCV**) are disclosed. Information derived from these sequences is useful in classification of viral isolates and in the development of immunochem. and nucleic acid reagents for detection of the virus and in vaccines.

L2 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1996:295079 CAPLUS

DOCUMENT NUMBER: 124:352673

TITLE: Recombinant production and purification of hepatitis C

virus **envelope** proteins for diagnostic and

INVENTOR(S) : therapeutic use  
 Maertens, Geert; Bosman, Fons; De Martynoff, Guy;  
 Buyse, Marie-Ange  
 PATENT ASSIGNEE(S) : Innogenetics N.V., Belg.  
 SOURCE: PCT Int. Appl., 146 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9604385	A2	19960215	WO 1995-EP3031	19950731
WO 9604385	A3	19960307		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2172273	AA	19960215	CA 1995-2172273	19950731
AU 9533824	A1	19960304	AU 1995-33824	19950731
AU 708174	B2	19990729		
EP 721505	A1	19960717	EP 1995-930434	19950731
EP 721505	B1	20020508		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09503396	T2	19970408	JP 1995-506189	19950731
BR 9506059	A	19971028	BR 1995-6059	19950731
AT 217345	E	20020515	AT 1995-930434	19950731
EP 1211315	A1	20020605	EP 2002-3643	19950731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 6150134	A	20001121	US 1996-612973	19960311
US 6245503	B1	20010612	US 1997-927597	19970911
PRIORITY APPLN. INFO.:				
			EP 1994-870132	A 19940729
			EP 1995-930434	A3 19950731
			WO 1995-EP3031	W 19950731
			US 1996-612973	A3 19960311
TI	Recombinant production and purification of hepatitis C virus envelope proteins for diagnostic and therapeutic use			
SO	PCT Int. Appl., 146 pp. CODEN: PIXXD2			
IN	Maertens, Geert; Bosman, Fons; De Martynoff, Guy; Buyse, Marie-Ange			
AB	<b>Envelope</b> proteins E1 and E2 of hepatitis C virus (HCV), their recombinant prodn. and purifn., their fragments and engineered derivs., their antigenic epitope peptides, their monoclonal antibodies, and their use for diagnostic and therapeutic means are provided. A method			
	is described for purifying recombinant HCV single or specific oligomeric <b>envelope</b> proteins, characterized in that upon lysing the transformed host cells to isolate the recombinantly expressed protein a disulfide bond cleavage or redn. step is carried out with a disulfide bond cleavage agent (such as dithiothreitol and/or Empigen BB) and an SH group protecting agent (such as N-ethylmaleimide). Various forms of the E1 and E2 proteins are constructed by std. genetic techniques using vaccinia virus recombination vectors; such proteins are specific for various HCV genotypes, may delete the hydrophobic region from			

E1, or remove various glycosylation sites; they may also add factor Xa cleavage sites and His6 tags for improved purifn. Epitope (such as F, G, H, and I) peptides are used to generate monoclonal antibodies and to monitor disease progression in patients. Furthermore, the **HCV** E1 protein and peptides are used for prognosing and monitoring the clin. effectiveness and/or clin. outcome of **HCV** treatment.

L2 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:872888 CAPLUS

DOCUMENT NUMBER: 123:307536

TITLE: In vivo transfection of hepatitis C virus complementary DNA into rodent liver by asialoglycoprotein receptor mediated gene delivery  
AUTHOR(S): Yamamoto, Masato; Hayashi, Norio; Miyamoto, Yasuhide; Takehara, Tetsuo; Mita, Eiji; Seki, Makoto; Fusamoto, Hideyuki; Kamada, Takenobu

CORPORATE SOURCE: School Medicine, Osaka University, Osaka, 565, Japan  
SOURCE: Hepatology (Philadelphia) (1995), 22(3), 847-55

CODEN: HPTLD9; ISSN: 0270-9139

DOCUMENT TYPE: Journal

LANGUAGE: English

TI In vivo transfection of hepatitis C virus complementary DNA into rodent liver by asialoglycoprotein receptor mediated gene delivery

SO Hepatology (Philadelphia) (1995), 22(3), 847-55

CODEN: HPTLD9; ISSN: 0270-9139

AU Yamamoto, Masato; Hayashi, Norio; Miyamoto, Yasuhide; Takehara, Tetsuo; Mita, Eiji; Seki, Makoto; Fusamoto, Hideyuki; Kamada, Takenobu

AB An in vivo model of hepatitis C virus (**HCV**) infection is needed to enable investigation of the mechanism of the liver injury that it causes. In this study, we used asialoglycoprotein receptor mediated gene delivery to obtain expression of the complementary DNA (cDNA) coding the core and part of the **envelope 1** protein of **HCV** because selective delivery to the hepatocytes has been reported to be attained with this method. The optimum carrier-DNA ratio was examd.

using

in vitro transfection and found to be important for the efficiency of this

method. In transfection in vivo, microautoradiog. examn. showed that the transfected plasmids were delivered selectively to the liver parenchymal cells. To obtain an immunohistochem. detectable level of protein expression in rodent liver, some modifications for increasing the in vivo transfection efficiency were performed; a lysosomal enzyme inhibitor, chloroquine, was used and the administration route of the carrier-DNA complex was changed from the tail vein to the portal vein. On the bases of these results, in vivo transfection with expression vector of **HCV** core/E1 region was performed. In rat liver transfected by intraportal injection with chloroquine, the transcript RNA and the core protein were detected. These results indicated that the **HCV** core/E1 expression vector was not merely delivered but also successfully expressed in the liver using asialoglycoprotein receptor mediated gene delivery. The no. of the **HCV** core expressing cells in the transfected liver was similar to that in patients with hepatitis C.

These

in vivo transfected animals should be useful for investigating the role of

this region in the liver injury caused by **HCV**.

L2 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:556035 CAPLUS

DOCUMENT NUMBER: 122:310542

TITLE: Classification of hepatitis C virus into major types and subtypes based on molecular evolutionary analysis  
AUTHOR(S): Ohba, Ken-ichi; Mizokami, Masashi; Ohno, Tomoyoshi; Suzuki, Kaoru; Orito, Etsuro; Ina, Yasuo; Lau, Johnson

CORPORATE SOURCE: Y. N.; Gojobori, Takashi  
Second Department of Internal Medicine, Nagoya City University Medical School, Kawasumi, Mizuho, Nagoya, 467, Japan

SOURCE: Virus Res. (1995), 36(2-3), 201-14  
CODEN: VIREDF; ISSN: 0168-1702

DOCUMENT TYPE: Journal

LANGUAGE: English

TI Classification of hepatitis C virus into major types and subtypes based on

SO molecular evolutionary analysis  
Virus Res. (1995), 36(2-3), 201-14  
CODEN: VIREDF; ISSN: 0168-1702

AU Ohba, Ken-ichi; Mizokami, Masashi; Ohno, Tomoyoshi; Suzuki, Kaoru; Orito, Etsuro; Ina, Yasuo; Lau, Johnson Y. N.; Gojobori, Takashi

AB Mol. evolutionary anal. was applied to det. the no. of hepatitis C virus (

HCV) types and subtypes based on all the HCV nucleotide sequences available from the DNA data banks (DDBJ, GenBank (NCBI), EMBL) and the literature. There was an excellent concordance among the types and subtypes assigned based on different HCV genomic regions. Only one HCV isolate was assigned to different HCV types based on the 5' non-coding (NC) and envelope 1 (E1) regions. The 5' NC region was well conserved and could be used to assign only types and not subtypes. From the sequence data available there were 13 subtypes based on the core region and 14 subtypes based on the E1 and non-structural protein 5 (NS5) regions.

L2 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:209827 CAPLUS

DOCUMENT NUMBER: 122:156064

TITLE: Hepatitis C virus variants from Vietnam are classifiable into the seventh, eighth, and ninth

major genetic groups

AUTHOR(S): Tokita, Hajime; Okamoto, Hiroaki; Tsuda, Fumio; Song, Pham; Nakata, Susumu; Chosa, Tohru; Iizuka, Hisao; Mishiro, Shunji; Miyakawa, Yuzo; Mayumi, Makoto

CORPORATE SOURCE: Immunol. Div., Jichi Med. Sch., Tochigi-Ken, Japan

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1994), 91(23), 11022-6

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

TI Hepatitis C virus variants from Vietnam are classifiable into the seventh,

SO eighth, and ninth major genetic groups

Proc. Natl. Acad. Sci. U. S. A. (1994), 91(23), 11022-6  
CODEN: PNASA6; ISSN: 0027-8424

AU Tokita, Hajime; Okamoto, Hiroaki; Tsuda, Fumio; Song, Pham; Nakata, Susumu; Chosa, Tohru; Iizuka, Hisao; Mishiro, Shunji; Miyakawa, Yuzo; Mayumi, Makoto

AB Thirty-four (41%) of 83 hepatitis C virus (HCV) isolates from com. blood donors in Vietnam were not classifiable into genotype I/1a, II/1b, III/2a, IV/2b, or V/3a; for 15 of them, the sequence was detd. for

1.6 kb in the 5'-terminal region and 1.1 kb in the 3'-terminal region. Comparison of the 15 Vietnamese isolates among themselves and with reported full or partial **HCV** genomic sequences indicated that they were classifiable into 4 major groups (groups 6-9) divided into 6 genotypes (6a, 7a, 7b, 8a, 8b, and 9a). Vietnamese **HCV** isolates of genotypes 7a, 7b, 8a, 8b, and 9a were significantly different from those classified into groups 4, 5, and 6 based on divergence within partial sequences; those of genotype 6a were homologous to a Hong Kong isolate (HK2) of genotype 6a. Phylogenetic trees based on the **envelope 1** (E1) gene (576 bp) of 55 isolates and a part of the nonstructural 5 (NS5) region (1093 bp) of 43 isolates revealed 9 major groups, 3 of which (groups 7, 8, and 9) were identified only in Vietnamese blood donors. With a prospect that many more **HCV** isolates with significant sequence divergence will be reported from all over the world, the domain of the **HCV** genome to be compared and criteria for grouping/typing and genotyping/subtyping will have to be detd., so that they may be correlated with virol., epidemiol., and clin. characteristics.

L2 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:673420 CAPLUS

DOCUMENT NUMBER: 121:273420

TITLE: Sequence analysis of the core gene of 14 hepatitis C virus genotypes

AUTHOR(S): Bukh, Jens; Purcell, Robert H.; Miller, Roger H.

CORPORATE SOURCE: Lab. Infectious Dis., Natl. Inst. Allergy Infectious Dis., Bethesda, MD, 20892, USA

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1994), 91(17), 8239-43

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

TI Sequence analysis of the core gene of 14 hepatitis C virus genotypes

SO Proc. Natl. Acad. Sci. U. S. A. (1994), 91(17), 8239-43

CODEN: PNASA6; ISSN: 0027-8424

AU Bukh, Jens; Purcell, Robert H.; Miller, Roger H.

AB We previously sequenced the 5' noncoding region of 44 isolates of hepatitis C virus (**HCV**), as well as the **envelope 1** (E1) gene of 51 **HCV** isolates, and provided evidence for the existence of at least 6 major genetic groups consisting of at least 12 minor genotypes of **HCV** (i.e., genotypes I/1a, II/1b, III/2a, IV/2b, 2c, V/3a, 4a-4d, 5a, and 6a). We now report the complete nucleotide sequence of the putative core (C) gene of 52 **HCV** isolates that represent all of these 12 genotypes as well as two addnl. genotypes provisionally designated 4e and 4f that we identified in this study. The phylogenetic anal. of the C gene sequences was in agreement with that of the E1 gene sequences. A major division in the genetic distance was obsd. between **HCV** isolates of genotype 2 and those of the other genotypes in anal. of both the E1 and C genes. The C gene sequences of 9 genotypes have not been reported previously (i.e., genotypes 2c, 4a-4f, 5a, and 6a). Our anal. indicates that the C gene-based methods currently used to det. the **HCV** genotype, such as PCR with genotype-specific primers, should be revised in light of these

data. We found that the predicted C gene was exactly 573 nt long in all 52 **HCV** isolates, with an N-terminal start codon and no in-frame stop codons. The nucleotide and predicted amino acid identities of the C gene sequences were in the range of 79.4-99.0% and 85.3-100%, resp. Furthermore, we mapped universally conserved, as well as genotype-specific, nucleotide and deduced amino acid sequences of the C



gene. The predicted C proteins of the different **HCV** genotypes shared the following features: (1) high content of proline residues, (2) high content of arginine and lysine residues located primarily in three domains with 10 such residues invariant at positions 39-62, (3) a cluster of 5 conserved tryptophan residues, (4) two nuclear localization signals and a DNA-binding motif, (5) a potential phosphorylation site with a serine-proline motif, and (6) three conserved hydrophilic domains that have been shown by others to contain immunogenic epitopes. Thus, we have extended anal. of the predicted C protein of **HCV** to all of the recognized genotypes, confirmed the existence of highly conserved regions of this important structural protein, and demonstrated that the genetic relatedness of **HCV** isolates is equiv. when analyzing the most conserved (i.e., C) and the most variable (i.e., E1) genes of the **HCV** genome.

L2 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:126371 CAPLUS

DOCUMENT NUMBER: 120:126371

TITLE: At least 12 genotypes of hepatitis C virus predicted by sequence analysis of the putative E1 gene of isolates collected worldwide

AUTHOR(S): Bukh, Jens; Purcell, Robert H.; Miller, Roger H.

CORPORATE SOURCE: Lab. Infect. Dis., Natl. Inst. Allergy Infect. Dis., Bethesda, MD, 20892, USA

SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1993), 90(17), 8234-8

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

TI At least 12 genotypes of hepatitis C virus predicted by sequence analysis of the putative E1 gene of isolates collected worldwide

SO Proc. Natl. Acad. Sci. U. S. A. (1993), 90(17), 8234-8

CODEN: PNASA6; ISSN: 0027-8424

AU Bukh, Jens; Purcell, Robert H.; Miller, Roger H.

AB In a previous study the authors sequenced the 5' noncoding (NC) region of 44 isolates of hepatitis C virus (**HCV**) and identified heterogeneous domains that provided evidence for addnl. genetic groups of **HCV** not previously recognized. In this study the authors have detd. the complete nucleotide sequence of the putative **envelope** 1 (E1) gene in 51 **HCV** isolates from around the world and found that they could be grouped into at least 12 distinct genotypes.

The E1 gene sequence of 8 of these genotypes has not been reported previously.

Although the genetic relatedness of **HCV** isolates detd. by the previous anal. of the 5' NC region predicted the relationships obsd. in the E1 gene, anal. of the 5' NC sequence alone did not accurately predict all **HCV** genotypes. The nucleotide and amino acid sequence identities of the E1 gene among **HCV** isolates of the same genotype were in the range of 88.0-99.1% and 89.1-98.4%, resp., whereas those of **HCV** isolates of different genotypes were in the range of 53.5-78.6% and 49.0-82.8%, resp. The latter differences are similar to

those found when comparing the **envelope** gene sequences of the various serotypes of the related flaviviruses as well as other RNA viruses. The authors found that some genotypes of **HCV** were widely distributed around the world, whereas others were identified only in discrete geog. regions. Four genotypes were identified exclusively in Africa and comprised the majority of **HCV** isolates on that continent. The E1 gene was exactly 576 nucleotides in length in all 51

- HCV** isolates with no in-frame stop codons. Anal. of the predicted E1 protein identified several conserved domains that may be important for maintaining its biol. function: (1) eight invariant cysteine residues,
- (2) three potential N-linked glycosylation sites, (3) a domain of nine amino acids (GHRMAWDMM), and (4) an amino acid doublet (GV) near the putative cleavage site at the C terminus of the protein. In conclusion, the discovery of at least 12 genotypes of **HCV** has important implications for **HCV** diagnosis and vaccine development.

L2 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:667866 CAPLUS

DOCUMENT NUMBER: 119:267866

TITLE: Suppression of hepatitis B virus expression and replication by hepatitis C virus core protein in

HuH-7

cells

AUTHOR(S): Shih, Chwen Ming; Lo, Szecheng J.; Miyamura, Tatsuo; Chen, Shiow Yi; Lee, Yan Hwa Wu

CORPORATE SOURCE: Inst. Biochem., Natl. Yang-Ming Med. Coll., Taipei, 112, Taiwan

SOURCE: J. Virol. (1993), 67(10), 5823-32

CODEN: JOVIAM; ISSN: 0022-538X

DOCUMENT TYPE: Journal

LANGUAGE: English

TI Suppression of hepatitis B virus expression and replication by hepatitis C

virus core protein in HuH-7 cells

SO J. Virol. (1993), 67(10), 5823-32

CODEN: JOVIAM; ISSN: 0022-538X

AU Shih, Chwen Ming; Lo, Szecheng J.; Miyamura, Tatsuo; Chen, Shiow Yi; Lee, Yan Hwa Wu

AB Hepatitis B and C viruses (HBV and **HCV**, resp.) are assocd. with acute and chronic liver diseases and hepatocellular carcinoma. To elucidate the mol. status of superinfection with these two hepatitis viruses, the authors cotransfected the full-length or truncated version

of

**HCV** structural genes (core and envelope 1)

together with the cloned HBV DNA into a human hepatoma cell line (HuH-7). Expression of HBV-specific major transcripts (3.5 and 2.1 kb), as well as HBV antigens (hepatitis B surface antigen and hepatitis B e and core antigens), was reduced about two- to fourfold by the presence of the **HCV** structural genes. In addn., the secretion of HBV viral particles, including the viral nucleocapsid and mature virion, was drastically suppressed about 20-fold. Anal. of the intracellular HBV

core

protein-assocd. nucleic acid indicated that the encapsidated HBV pregenomic RNA was similarly reduced about 14-fold. Deletion anal. of

the

**HCV** structural genes demonstrated that the core gene alone or the fragment contg. the core protein's N-terminal 122 amino acid residues conferred the same level of suppressive activity as the full-length structural genes. By indirect immunofluorescence, the authors found that the core protein of **HCV** was located in the cytoplasm of transfected HuH-7 cells at day 3 posttransfection and was targeted to the nucleus at day 6. Thus, the kinetics of the suppressive effect exerted

by

**HCV** constructs matched the timing of core protein entrance into the nucleus. The authors' results substantiate the clin. finding that

HBV

markers are suppressed by superinfection with **HCV** and further imply that this inhibitory effect may occur in the processes of transcription and encapsidation of HBV pregenomic RNA and may be mediated by the core protein of **HCV**. The deduced amino acid sequence of the **HCV** core protein has revealed that it is a basic protein which contains a putative DNA-binding motif (SPRG), as well as triplicate nuclear localization signals and several putative protein kinase A and C recognition sites. These characteristics imply that the **HCV** core protein can also function as a gene-regulatory protein.

L2 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:601360 CAPLUS

DOCUMENT NUMBER: 119:201360

TITLE: Antigenic regions within the hepatitis C virus **envelope 1** and non-structural proteins: Identification of an IgG3-restricted recognition site within the **envelope 1** protein

AUTHOR(S): Sallberg, M.; Ruden, U.; Wahren, B.; Magnus, L. O.

CORPORATE SOURCE: Dep. Virol., Karolinska Inst., Stockholm, Swed.

SOURCE: Clin. Exp. Immunol. (1993), 91(3), 489-94

CODEN: CEXIAL; ISSN: 0009-9104

DOCUMENT TYPE: Journal

LANGUAGE: English

TI Antigenic regions within the hepatitis C virus **envelope 1** and non-structural proteins: Identification of an IgG3-restricted recognition site within the **envelope 1** protein

SO Clin. Exp. Immunol. (1993), 91(3), 489-94

CODEN: CEXIAL; ISSN: 0009-9104

AU Sallberg, M.; Ruden, U.; Wahren, B.; Magnus, L. O.

AB Antibody binding to antigenic regions of hepatitis C virus (**HCV**)

**envelope 1** (E1; residues 183-380), E2/non-structural

(NS) 1 (residues 380-437), NS1 (residues 643-690), and NS4 (1684-1751)

proteins were assayed with 50 sera for antibodies to **HCV** (anti-

**HCV**) and with 46 sera without anti-**HCV**. Thirty-four

peptides, 18 residues long with an eight-amino acid overlap within each

**HCV** region, were synthesized and tested with all 96 sera. Within

the E region 183-380, the major binding site was located to residues

203-220, and was recognized by eight sera. Within the E2/NS1 region

380-437, the peptide covering residues 410-427 was recognized by two

sera,

and within the NS1 region 643-690, peptides covering residues 663-690

were

recognized by four sera. Within the NS4 region 1684-1751, 27 sera were

reactive to one or more of the NS4 peptides, and 21 out of these were

reactive with peptide 1694-1711. One part of the major binding site

could

be located to residues 1701-1704, with the sequence Leu-Tyr-Arg-Glu. The

IgG1, IgG3 and IgG4 subclasses were reactive with the five antigenic

regions of **HCV** core, residues 1-18, 11-28, 21-38, 51-68 and

101-118. Reactivity to the major **envelope** site consisted almost

exclusively of IgG3, and reactivity to the major site of NS4 consisted

only of IgG1. Thus, a non-restricted IgG response to linear **HCV**

-encoded binding sites was found to the core protein, whereas IgG

subclass-restricted linear binding sites were found within the E1

protein,

and within the NS4 protein.

L2 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:510547 CAPLUS  
 DOCUMENT NUMBER: 119:110547  
 TITLE: Hepatitis C virus (HCV) genomic sequences  
 for diagnostics and therapeutics  
 INVENTOR(S): Cha, Taian; Beall, Eileen; Irvine, Bruce; Kolberg,  
 Janice; Urdea, Michael S.  
 PATENT ASSIGNEE(S): Chiron Corp., USA  
 SOURCE: PCT Int. Appl., 186 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9219743	A2	19921112	WO 1992-US4036	19920508
WO 9219743	A3	19931125		
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
AU 9221558	A1	19921221	AU 1992-21558	19920508
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				
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PRIORITY APPLN. INFO.:			US 1991-697326	A 19910508
			CS 1993-2377	A3 19920508
			US 1992-881528	B1 19920508
			WO 1992-US4036	A 19920508
			US 1994-221653	A3 19940401
TI	Hepatitis C virus (HCV) genomic sequences for diagnostics and therapeutics			
SO	PCT Int. Appl., 186 pp. CODEN: PIXXD2			
IN	Cha, Taian; Beall, Eileen; Irvine, Bruce; Kolberg, Janice; Urdea, Michael S.			
AB	The cDNA probe sequences for the NS5, envelope 1, 5'UT, and the core regions of 5 genotypes of HCV are given. These cDNA probes can be used for detection of HCV by e.g. sandwich hybridization. Also they can be used for prep. antigenic peptides for induction of antibodies to HCV for the title purposes.			

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LOGOFF? (Y)/N/HOLD:y

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